K112422

IMMY

MAR 2 8 2012

510(k) Summary
CrAg Lateral Flow Assay

This 510(k) summary is submitted in accordance with 21 CFR §807.92

Owner: Immuno-Mycologics, Inc.
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Contact: Dr. Sean K. Bauman, President & CEO
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Prepared: March 26, 2012

Trade Name: CrAg Lateral Flow Assay

Common Name: Cryptococcal Antigen Lateral Flow Immunoassay

Regulation: 866.3165

Predicate Device: Immuno-Mycologics' CrAg Lateral Flow Assay (K102286)

Intended Use: The CrAg Lateral Flow Assay is an immunochromatographic test system for the qualitative or semi-quantitative detection of capsular polysaccharide antigens of *Cryptococcus* species complex (*Cryptococcus neoformans* and *Cryptococcus gatti*) in serum and cerebral spinal fluid (CSF).

The CrAg Lateral Flow Assay is a prescription-use laboratory assay, which can aid in the diagnosis of Cryptococcosis.

Device Description:
Explanation:

Detection of cryptococcal antigen in serum and CSF has been used for over forty years to aid in the diagnosis of cryptococcosis with very high sensitivity and specificity (9,14,15). Current guidelines for the management of cryptococcal disease partially base treatment recommendations on cryptococcal antigen presence and more specifically on cryptococcal antigen titers (16).

Cryptococcosis is caused by both species of the *Cryptococcus* species complex (*Cryptococcus neoformans* and *Cryptococcus gatti*) (5,6,12,13). Individuals with impaired cell-mediated

immune (CMI) function due to acquired immunodeficiency syndrome (AIDS) (19), lymphoproliferative disorders (18), steroid therapy (8), and organ transplantation (7) are at increased risk of cryptococcosis. AIDS accounts for 80-90% of cryptococcal infections (11). The incidence of cryptococcosis in AIDS patients in the United States is estimated to be 5-10% (11), while the incidence of cryptococcosis in other parts of the world, such as Africa, is as high as 30% (3). Cryptococcosis is the fourth most common opportunistic, life-threatening infection among AIDS patients (10).

Description:

The CrAg Lateral Flow Assay is a dipstick sandwich immunochromatographic assay, which detects cryptococcal antigen in serum and CSF. For the qualitative procedure, specimens are diluted 1:2 in 1x Specimen Diluent and analyzed. For the semi-quantitative procedure, specimens are diluted 1:5 in 1x Specimen Diluent followed by 1:2 serial dilutions. All dilutions are then analyzed as in the qualitative procedure. Specimens are placed into an appropriate reservoir, such as a test tube or microtiter plate, and the lateral flow device is then placed into the reservoir allowing the specimen to come into contact with the test membrane. The test uses specimen wicking to capture gold-conjugated, anti-cryptococcal monoclonal antibodies and gold-conjugated control antibodies that are deposited onto a membrane. If cryptococcal antigen is present in the specimen, it binds to the gold–conjugated, anti-cryptococcal antibodies. The gold-labeled antibody-antigen complex will continue to wick up the membrane where it will interact with the Test Line (T). The Test Line is immobilized anti-cryptococcal monoclonal antibodies. If the specimen contains cryptococcal antigen, a sandwich is created with the gold-labeled antibodies and the immobilized antibodies, causing a visible line to develop at the test line site (T). If proper flow occurs and the reagents are reactive at the time of use, the wicking of any specimen, positive or negative, will cause the gold-conjugated control goat IgG antibody to move to the Control Line (C) which is immobilized bovine anti-goat IgG antibody. The immobilized anti-goat antibody will bind to the gold-conjugated goat IgG Control antibody and will cause a visible line to develop (C). A positive test result will create two lines, while a negative test result will create one line (Figure 1). If the control line fails to develop a line, then the test is not valid.

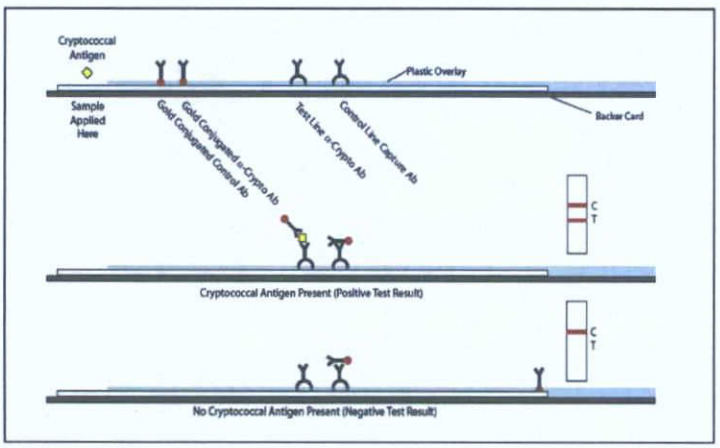

Figure 1. CrAg Lateral Flow Assay Schematic

Technological Characteristics Summary

A comparison between the CrAg LFA and the CrAg LFA (K102286 - Serum only) is presented in Table 1.

Table 1. Comparison with Predicate Device

SIMILARITIES		
Feature	CrAg LFA (New Device)	CrAg LFA (Serum Only) (K102286)
Intended Use		
Intended Use	Immunochromatographic test system for the qualitative or semi-quantitative detection of the capsular polysaccharide antigens of *Cryptococcus* species complex (*Cryptococcus neoformans* and *Cryptococcus gattii)* in serum	Immunochromatographic test system for the qualitative or semi-quantitative detection of the capsular polysaccharide antigens of *Cryptococcus* species complex (*Cryptococcus neoformans* and *Cryptococcus gattii)* in serum
Indication For Use	Prescription-use laboratory assay, which can aid in the diagnosis of cryptococcosis	Prescription-use laboratory assay, which can aid in the diagnosis of cryptococcosis
Device Description		
Technology	Lateral Flow Assay	Lateral Flow Assay
Sample Matrix	Serum	Serum
Instruments	None	None
Assay Components	Specimen diluent, lateral flow strips, built-in control, gold conjugated antibodies	Positive control, negative control, latex cards, latex conjugated antibodies
Specimen Pre-Treatment	Dilution	Dilution
Detection Antibody	Anti-cryptococcal monoclonal antibody	Anti-cryptococcal monoclonal antibody
Storage Requirements	20-25°C	20-25°C
DIFFERENCES		
Feature	Cryptococcal Antigen Lateral Flow Assay	Latex-*Cryptococcus* Antigen Detection System
Intended Use		
Intended Use	Test for the qualitative or semi-quantitative detection of capsular polysaccharide antigens of *Cryptococcus* in serum	Test for the qualitative or semi-quantitative detection of capsular polysaccharide antigens of *Cryptococcus* in serum and CSF
Indication For Use	No differences	No differences

Performance Summary

A. Precision Studies (Repeatability & Reproducibility)

Serum repeatability and reproducibility results can be found in the predicate device 510(k) (K102286)

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Repeatability and reproducibility with CSF specimens were determined by spiking a mock CSF that was negative by the IMMY Latex-*Cryptococcus* Antigen Detection System with cryptococcal antigen at four concentrations: Negative, high negative (C_5), low positive (near C_{95}), and medium positive. The samples were analyzed on the CrAg Lateral Flow Assay in triplicate on five different days, at three different sites with a total of five different operators, on one lot, according to EP5-A2. One site was internal (Site 1) and the remaining two were a US reference laboratory (Site 2) and a US hospital laboratory (Site 3). For repeatability, percent positive and percent negative detected were calculated for each site (Table 2). For reproducibility, overall percent positive and percent negative detected were calculated by combining the data from all three sites (last two rows of Table 2).

Table 2. Repeatability at 3 Different Sites

	CSF							
Sample	1		2		3		4	
	Med. Pos		Low Pos		High Neg		Neg	
Neg/Pos	-	+	-	+	-	+	-	+
Site 1	0	30	0	30	27	3	30	0
Percent %	0	100	0	100	90	10	100	0
Site 2	0	30	0	30	30	0	30	0
Percent %	0	100	0	100	100	0	100	0
Site 3	0	15	0	15	15	0	15	0
Percent %	0	100	0	100	100	0	100	0
Total No.	0	75	0	75	72	3	75	0
Percent %	0	100	0	100	96	4	100	0

B. Analytical Sensitivity (lower limits of the assay/analytical cut-off)

Serum analytical sensitivity can be found in the predicate device 510(k) (K102286)

Analytical sensitivity for the CrAg Lateral Flow Assay was estimated by running 24 replicates of varying concentrations of cryptococcal antigen diluted in mock CSF on one lot of kits, according to EP12-A2. The analytical cut-off was defined as the concentration where 50% of the results were positive and 50% of the results were negative. The analytical cut-off is 1.25ng/ml.

C. Analytical Specificity (cross-reactivity)

Serum analytical specificity can be found in the predicate device 510(k) (K102286)

Due to specimen availability, the following CSF conditions were not tested in the CrAg Lateral Flow Assay: *S. pneumonia, Enterovirus, Enterobacteriaceae, Streptococcus* spp., *Staphylococcus* spp., *diphtheroid, H. influenzae* type B, *N. meningitidis, Enterococcus* spp., *Epstein Barr, Herpes simplex virus* Type 1 and 2, *Listeria monocytogenes, Trichosporon beigelii, and* samples with syneresis fluid condensation.

This assay was not evaluated for potential interference related to specimen pretreatment with 2-mercaptoethanol or with specimens including the following subastances or conditions: bloody CSF, cloudy CSF, white blood cells, xanthochromic CSF, bilirubin, protein, systemic lupus erythmatosus (SLE), sarcoidosis, or *N. memingitides.*

D. Linearity

N/A

E. High Dose Hook Effect

High dose hook effect concentrations with specimens were determined by spiking negative serum that was negative by the IMMY Latex-*Cryptococcus* Antigen Detection System and CrAg Lateral Flow Assay, with cryptococcal antigen at various concentrations between 20 and 500ug/ml. Each concentration was tested in triplicate at IMMY on one lot of CrAg Lateral Flow Assay, according to the package insert. It was determined that serum specimens with a cryptococcal antigen concentration higher than 200ug/ml can produce a high dose hook effect and therefore may produce a false negative result.

F. Method Comparisons

Predicate Device Method Comparison

Not Applicable

Other Method Comparison – Culture/India Ink (Gold Standards)

Serum method comparison to gold standards can be found in the predicate device 510(k) (K102286)

The CrAg Lateral Flow Assay was compared to the gold standard for the diagnosis of cryptococcosis (culture and/or India Ink) to evaluate the sensitivity and specificity of the assay in CSF. These studies contained a mix of both prospective and retrospective specimens. A summary of the data collected is included in Tables 3 and 4 below:

Table 3. CSF 2x2 Contingency Table: Culture/India Ink

		Culture/India Ink	
		Positive	Negative
CrAg LFA Assay	Positive	65	0
	Negative	0	99

Table 4. CSF Statistical Analysis: Culture/India Ink

	Calculated	95% CI
Sensitivity	100%	94.4-100.0%
Specificity	100%	96.3-100%

Conclusion

The information submitted in this premarket notification is complete and supports a substantial equivalence decision.

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

10903 New Hampshire Avenue
Silver Spring, MD 20993

MAR 2 8 2012

Immuno-Mycologics, Inc.
c/o Sean K. Bauman, Ph.D.
President and CEO
2700 Technology PL
Norman, OK 73071

Re: K112422
Trade/Device Name: CrAg Lateral Flow Assay (CrAg LFA)
Regulation Number: 21 CFR § 866.3165
Regulation Name: Cryptococcal antigen lateral flow assay
Regulatory Class: II
Product Code: GMD
Dated: March 26, 2012
Received: March 27, 2012

Dear Dr. Bauman:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice

requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

IMMY

Indications for Use Statement

510(k) Number (if known): K112422

Device Name: CrAg Lateral Flow Assay

Indications for Use:

The Cryptococcal Antigen Lateral Flow Assay (CrAg LFA) is an immunochromatographic test system for the qualitative or semi-quantitative detection of capsular polysaccharide antigens of *Cryptococcus* species complex (*Cryptococcus neoformans* and *Cryptococcus gattii*) in serum and cerebral spinal fluid (CSF).

The CrAg Lateral Flow Assay is a prescription-use laboratory assay, which can aid in the diagnosis of cryptococcosis.

Prescription Use X AND/OR Over-The-Counter Use_____
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Freddie W. Poole

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

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